Skin Physiology, Irritants, Dry Skin and Moisturizers

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Skin is a physical barrier to the environment. It is the alteration of the barrier properties and actual damage to this barrier that causes dryness and dermatitis when the skin is exposed to water, soaps, gloves, chemicals and harsh weather conditions. The repair of the damage by moisturizers is related to the physical and chemical interactions of the ingredients with the natural skin barrier.

Skin Physiology: Structure and Function Basics

Skin has two main structural layers—the epidermis and the dermis (Figure 1).

- The epidermis is the outer layer of skin, which serves as the physical and chemical barrier to the interior body and exterior environment.
- The dermis is the deeper layer providing the structural support of the skin.

Epidermis and Stratum Corneum: The Structure and Growth of Skin

The epidermis consists of stacked layers of cells in transition. Protein bridges called desmosomes connect the cells.

- The bottom layer of cells adjacent to the dermis are the basal cells which reproduce.
- As the cells mature, they move towards the outer layer of skin leading to terminal differentiation of the cells. During the process of maturation, the physiology, chemical composition, shape and orientation of the cells change.
- When the cells reach the top layer of skin—the stratum corneum—the cells are called corneocytes and are no longer viable. Corneocytes lack a nucleus and cellular structures.
- Corneocytes are flat, hexagonal-shaped cells filled with water-retaining keratin proteins surrounded by a protein envelope and lipids (Figure 2). The cellular shape and the orientation of the keratin proteins add strength to the stratum corneum. There are 10-30 layers of stacked corneocytes.
- The thicker skin on the palms and soles has the most layers of stacked corneocytes.
- The cells remain connected to each other by protein bridges called desmosomes. Stacked bilayers of lipids surround the cells in the extracellular space. The resulting structure is the natural physical and water-retaining barrier of the skin.

Fillagrin: The Breakdown of Skin

During the process of maturation, the viable cells moving towards the stratum corneum begin to clump proteins into granules.

- These granules are present in the granular cell layer of the skin and are filled with a protein called fillagrin.

- Fillagrin becomes complexed with keratin proteins in the granular cells. This complex protects fillagrin from proteolytic breakdown.
- As the degenerating cells move towards the outer layer of the skin, enzymes break down the keratin-fillagrin complex.
- Fillagrin is on the outside of the corneoctyes and water-retaining keratin remains inside the corneocytes of the stratum corneum.

When the moisture content of the skin is **decreased**, specific proteolytic enzymes in the stratum corneum are triggered to further break down fillagrin into free amino acids.

Natural Moisturizing Factors: The Natural Retention of Water in the Skin

The free amino acids, along with other physiological chemicals such as lactic acid, urea and salts, are present in the stratum corneum.

- Together these chemicals are called "natural moisturizing factors" and are responsible for keeping the skin moist and pliable by attracting and holding water—a property called hygroscopic.
- The water content of the stratum corneum is normally about 30%.
- The proteolytic breakdown of fillagrin to amino acids only happens when the skin is **dry** to control the osmotic pressure of the skin and the amount of water it holds. There is less need for breakdown of fillagrin in humid weather than in dry weather.

Generation of Natural Moisturizing Factors in the Skin

Maturation and differentiation of epidermal cells in the middle layer of skin
↓
Fillagrin protein clumps into granules in the granular cell layer
↓
Fillagrin becomes complexed to keratin protein to protect from proteolytic degradation
↓
Cells lose their normal cell contents and become protein envelopes filled with keratin/fillagrin proteins called corneocytes
↓
Corneocytes move towards the very outer layer skin
↓
Enzymes break down keratin/fillagrin complex to fillagrin and keratin
↓
Decreased water content stratum corneum
↓
Proteolytic enzymes activated
↓
Fillagrin degraded into individual amino acids
↓
Amino acids plus other chemicals form Natural Moisturizing Factors in stratum corneum
↓
Holds water to rehydrate stratum corneum

Desquamation (The Shedding of Skin Cells)

Desquamation is another important factor in keeping the skin smooth.

- Desquamation is the enzymatic process of dissolving the desmosomes, the protein connections between corneocytes, and the eventual shedding of these cells.
- Opposite to the production of amino acids from proteolytic degradation of fillagrin proteins, the proteolytic enzymes responsible for desquamation function in the presence of a **well-hydrated** stratum corneum. These enzymes are located intercellularly.
- In the absence of water, the cells do not desquamate normally and the result is thickened, dry, rough, scaly skin.
- There is a normal physiological balance in the production of corneoctyes and shedding. Increased production of corneocytes (skin diseases such as psoriasis) or decreased shedding (skin diseases like ichthyosis) results in the accumulation of cells on the skin surface and dry, rough skin.

Desquamation of Cells

Intact corneocytes in upper level of **hydrated stratum corneum**

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Proteolytic enzymes break protein connections between corneocytes

↓

Corneocytes desquamate

↓

Skin stays normal without dry scales

Intercellular Lipids

The last factor that is necessary in explaining how the natural skin barrier works to keep the skin moist and pliable is the function of the intercellular lipids.

- These lipids form stacked bilayers (multilamellae) surrounding the corneocytes in the stratum corneum and incorporate water into this architecture (Figure 3).
- The lipids are derived from the degradation of cells in the granular layer of skin (similar to the origin of the protein granules). Special lipid structures called lamellar granules are released into the extracellular spaces of the degrading cells. There is also release of lipids from the former cell membranes.
- These released lipids include cholesterol, free fatty acids and sphingolipids.
- Ceramide, a type of sphingolipid derived from the lamellar granules, is one of the major lipid components responsible for generating the stacked lipid structures. These lipids trap water molecules in their hydrophilic (water attracting) region.
- The newly formed stacked lipids surrounding the corneocytes provide an impermeable barrier for the passage of water out of the stratum corneum and the prevention of the natural moisturizing factors from leaching out of the surface layers of skin.
- There are sharp decreases in intercellular lipids after age 40 resulting in more susceptibility to dry skin conditions.

Intercellular Lipid Layers

Lipids in granular cell layer of skin form granules

↓

Degeneration of granular cells releases lipid granules into intercellular spaces

↓

Lipids released from degeneration of cells and lipid granules complex together to form intercellular stacked lipid structures

↓

Lipid layers hold water and surround corneocytes to provide permeability barrier

The intercellular lipids and corneocytes containing proteins and natural moisturizing factors work together to provide an efficient barrier against water loss and water retention to maintain the flexibility of the skin. The protective forces shield the skin from desiccation and environmental assaults.

Irritants and Damage to the Skin Barrier

The major factor responsible for dry, scaly skin and irritant dermatitis can be related to the loss of water from the stratum corneum.

- This loss of water is called transepidermal water loss (TEWL).
- The stratum corneum receives water from the dermis and some from the environment.
- Water is the "plasticizer" of the skin making it pliable and smooth.
- Numerous external factors can cause TEWL.
- The water content of the stratum corneum fluctuates with environmental humidity levels. There is accentuation of dry skin with exposure to cold, wind and low humidity.
- Other external factors damage the stratum corneum barrier by denaturing keratin protein, removing natural moisturizing factors and interrupting the lipid bilayers. These factors include solvents, detergents, excessive use of water and soap, and other irritating chemicals.
- The severity of the damage is dependent on the type and intensity of exposure to these irritating factors.

An irritant is any agent that is capable of producing cell damage if there is exposure for sufficient time and in sufficient concentrations.

- It may require repeated and prolonged exposure to see the actual damage.
- Anyone exposed to excessive amounts of cleaning agents and water--health care personnel, hairdressers, food service workers, bartenders, and dishwashers--may experience extreme changes in the health and nature of their skin.

Water is a weak irritant.

- Significant water exposure causes the loss of the soluble natural moisturizing factors and some of the protective lipids paradoxically resulting in TEWL.

- Persistent hydration of the skin from exposure to water results in:
    - penetration of foreign substances and contribute to allergic and irritant contact dermatitis and
    - changes in the normal ecological environment in/on the skin, which can support the overgrowth of pathological organisms on the skin.

Soaps and cleansers are considered mild irritants.

- These agents are beneficial surfactants that remove exogenous dirt, bacteria, skin oils, perspiration and crusts (desquamated skin cells).
- Repeated and prolonged exposure to these cleansers results in denatured skin proteins, disorganization of the lipid lamellae layers, removal of the protective intercellular lipids, loss of natural moisturizing factors and decreased cohesion between cells.
- The temperature of the water can increase the irritant capacity of skin cleansers by causing increased absorption of the cleanser with warmer temperatures. There is greater removal of the protective lipids with hotter water.
- The end result of prolonged use of water and cleansing agents is alteration of the water-holding capacity of the skin and an increased TEWL. Dry, scaly skin that is less pliable and damaged is the physical result.

There are also endogenous factors that make one more susceptible to damaged skin by external factors.

- These factors include having active skin disease such as psoriasis, eczema, inherited dry skin conditions (ichthyosis), a previous history of skin diseases (childhood eczema), sensitive skin and/or older age.
- These endogenous factors may exacerbate dryness of the skin and increase one's susceptibility to dermatitis.

In summary, the exposure to irritants with the resulting transepidermal water loss compromises the barrier function of the stratum corneum and decreases its ability to protect the skin against environmental influences.

- The harsher the cleansers or solvents, and/or prolonged exposure to irritants, the greater removal of protective lipids, proteins, natural moisturizing factors and water loss.
- With decreased water capacity, there is also loss of function of the normal enzymes to desquamate the corneocytes.
- If the water content of the skin is less than 10%, these interacting factors are disturbed and the result is dry, scaly, fissured and less pliable skin.

How Moisturizers Work

When the skin is damaged, repair is dependent on retarding the loss of moisture from the skin.

- Moisturizers are defined as chemicals that increase the water content of the stratum corneum and are hydrating agents.

- Moisturizers work by using ingredients that are occlusive and/or humectant agents.
- These ingredients are the same or similar to natural components in the skin (biomimetic).

Occlusive agents work by physically blocking the loss of water from the skin.

- These hydrophobic agents form an occlusive film on the skin that reduces TEWL by preventing evaporation of water from the stratum corneum.
- These agents may also help to restore the lipid barrier of the skin.
- Examples of occlusive agents include petrolatum, beeswax, lanolins and oils.

Humectant agents attract water to the skin.

- The water is drawn from the deeper dermis, rarely the environment.
- The hydration of the stratum corneum normalizes the intercellular lipids and the natural desquamation process.
- The skin becomes more resistant to drying conditions.
- Humectants mimic the role of natural hydrophilic humectants in the stratum corneum.
- These chemicals include amino acids, lactic acids, alpha hydroxy acids, propylene glycol, glycerine and urea.
- Some of these agents are the components of the skin's natural moisturizing factors.

"Barrier-repairing" moisturizers contain lipids that are similar to the intercellular lipids of the skin. The combinations of fatty acids, ceramide and cholesterol in the moisturizers may help to repair lipid bilayers affected by soaps, solvents and extreme dry, cold weather conditions by replacing key lipid components.

Moisturizers contain other ingredients besides humectants and/or occlusive agents.

- Ingredients may improve the skin's softness by lubricating and filling in the spaces between dry skin cells. An ingredient list on a moisturizer will list these agents as the "active" ingredients.
- The "inactive" ingredients solubilize, stabilize, emulsify, suspend and /or disperse ingredients in order to produce an aesthetically pleasing product.
- Most moisturizers contain 65-85% water in a lotion form with water acting as an agent to disperse the active and inactive ingredients. The high water content also serves to allow absorption of some components and evaporation of the moisturizer. The water acts as a temporary hydrating agent.
- Moisturizers in a cream form contain less water and more oils or occlusive agents.
- Ointments are oil-based compounds with a minimum amount or no water in the product. These products are usually very occlusive and greasy. An example would be pure petroleum jelly.

Summary

The unique structure of the stratum corneum of the skin contributes to its function as a barrier to water loss and the external harsh environment. The injury to this barrier by the environment and common irritants with the resulting loss of water from the skin is the main reason for the development of dry skin or irritant dermatitis. Moisturizers can help to increase the hydration of the skin and possibly repair/restore the barrier through use of chemicals that are similar to the skin's natural moisturizing factors or occlusion of the skin to prevent water loss.

Moisturizer Chemistry

Ingredients in Moisturizers	Action
Water: 65-85% (lotions and creams)	Dilutes and disperses ingredients, evaporates from skin surface
Lipids: 5-35% (lotions and creams) Up to 100% (ointments) (mineral oil, petrolatum, lanolin, beeswax, vegetable oils, cholesterol, fatty alcohols, fatty acids, ceramides)	Occlusive effect to prevent water loss, repair lipid layers, restore barrier
Emulsifiers: 1-2% (stearic acid, triethanolamine, quaternium 15, fatty alcohols)	Allow water and lipids to stay in suspension as a lotion form
"Active Ingredients": 0.05-15% (petrolatum 30-100%, glycerine, dimethicone, allantoin, urea, alpha hydroxy acids, lactic acid, sunscreens/sunblocks)	Attract water to the skin, skin protectants, lubricate, fill in spaces between cells, block UVA/UVB
Preservatives: 0.1 to 1% (parabens, quaternium 15, imidazolidyl urea, disodium EDTA, methylisothiazoline, alcohols)	Prevent growth of microorganisms in the product
Fragrance: <0.25%	Mask the odor of the lipids or give the product a fragrant scent

Moisturizer Terminology

Anti-aging: Sunscreen/sunblock in the product.

Barrier Cream: Alter the penetration of substances such as water and chemicals into the skin by interaction of the cream ingredients with the stratum corneum. A protective water-repellent film may form on the skin but continues to allow normal evaporation of water from the skin.

Dermatologist Tested: Does not mean anything of significance. Can use the term even if only one dermatologist tested the product.

Hypoallergenic: May have reduced amounts of chemicals that have an allergenic potential (fragrance, preservatives) but not a reliable term.

Non-comedogenic: The ingredients do not cause the pores on the face, chest or back to become blocked and develop comedones (blackheads). Testing of products may have been done on rabbit ears.

Oil in Water Emulsion: An oil is dissolved in water. This is a water-based product. These products are usually lotions or light creams and dissolve readily into the skin without leaving a greasy film.

Sensitive Skin Formula: There is no definition for this term. The product may have reduced fragrance or preservatives.

Therapeutic Effect: Restores the natural skin barrier to help the skin heal.

Unscented: No fragrance used in the product. The product may actually have a masking fragrance to decrease the odor of the oils in the products.

Water in Oil Emulsion: A small amount of water is dissolved in an oil-based product (petrolatum, mineral oil, natural plant oils). These products are usually heavier creams or ointments and can act as occlusive agents by forming a film on the skin.

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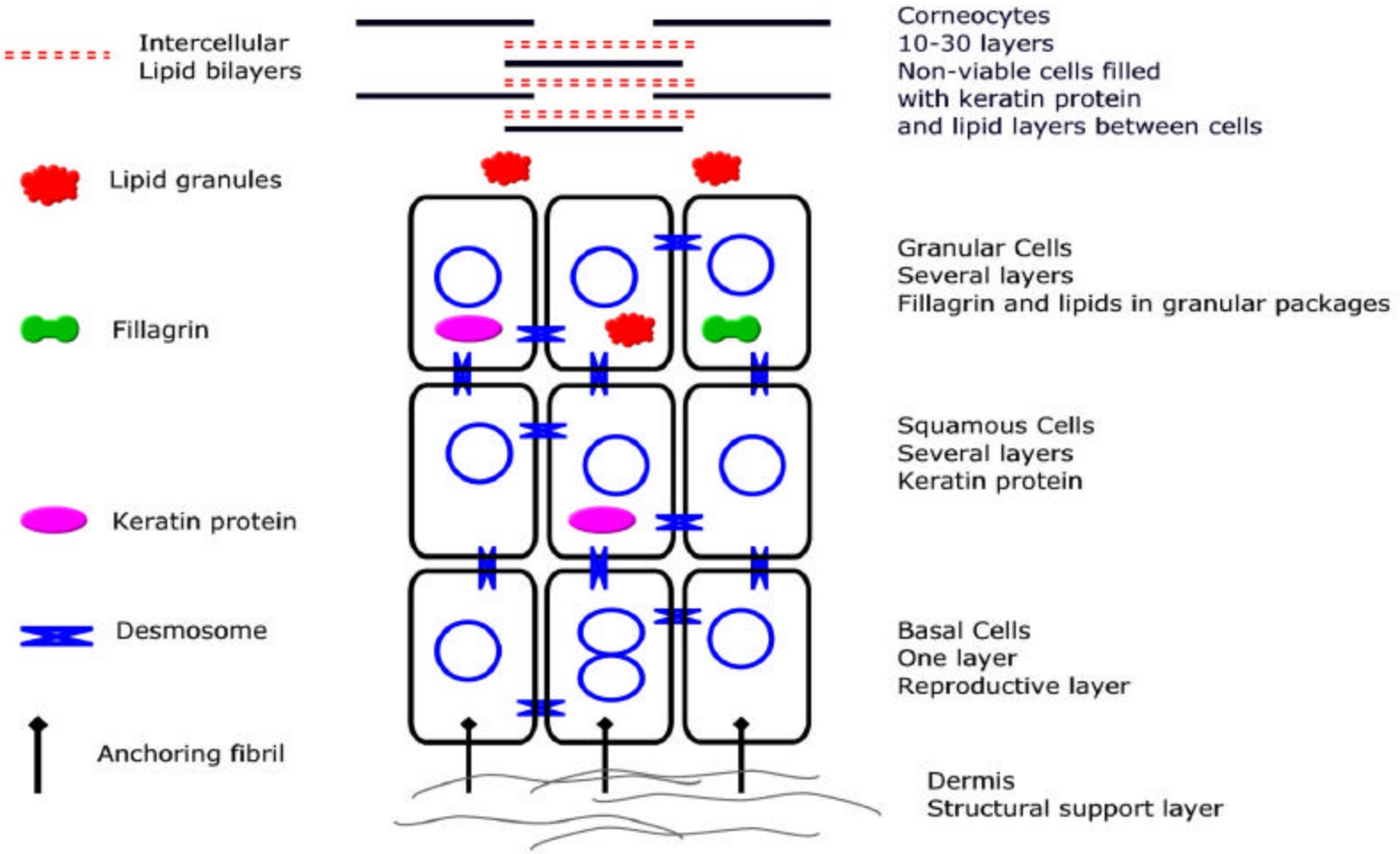

Figure 1. Structure of the Epidermis: Physical Skin Barrier

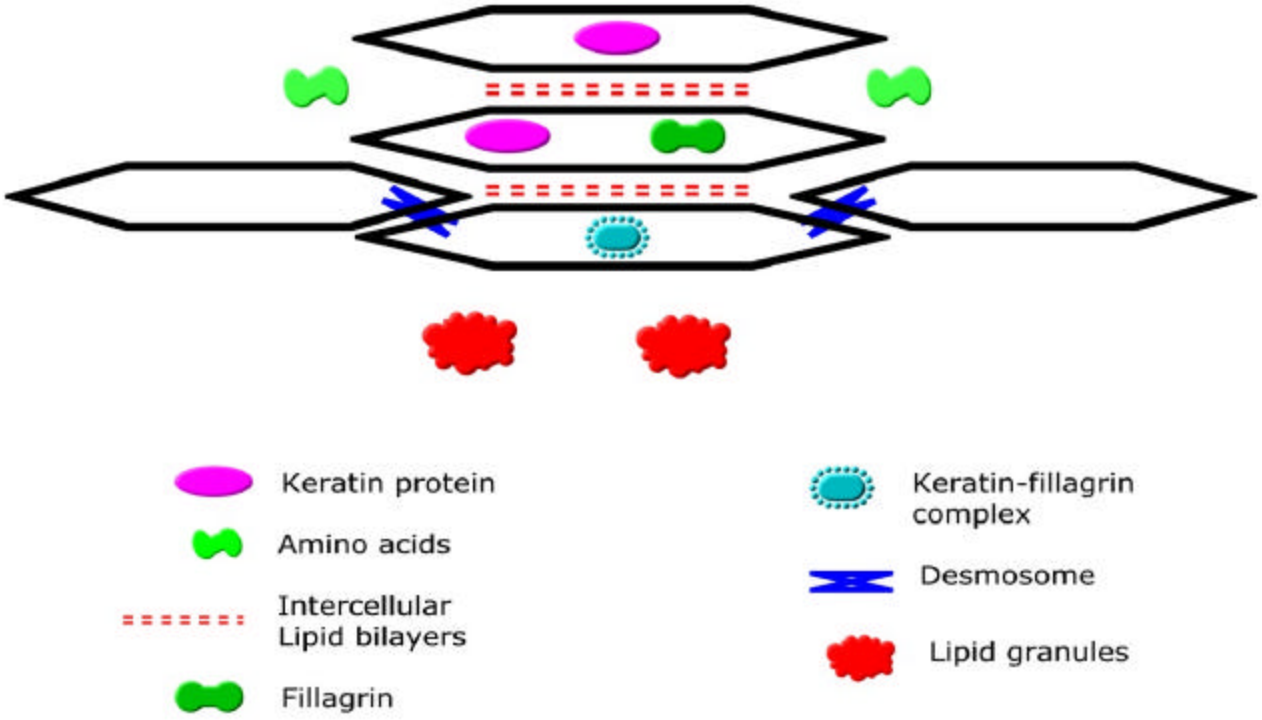

Figure 2. Physical Skin Barrier: Corneocyte Layer

Figure 3. Physical Skin Barrier:
Corneocyte-Lipid Bilayers